Introducing a nationwide registry: the Swiss study on aneurysmal subarachnoid haemorrhage (Swiss SOS)

Schatlo, B ; Fung, C ; Fathi, A-R ; Sailer, M ; Winkler, K ; Daniel, R T ; Bijlenga, P ; Ahlborn, P ; Seule, M ; Zumofen, D ; Reinert, M ; Woernle, C ; Stienen, M ; Levivier, M ; Hildebrandt, G ; Mariani, L ; Bernays, R ; Fandino, J ; Raabe, A ; Keller, E ; Schaller, K

Abstract: BACKGROUND: Aneurysmal subarachnoid haemorrhage (aSAH) is a haemorrhagic form of stroke and occurs in a younger population compared with ischaemic stroke or intracerebral haemorrhage. It accounts for a large proportion of productive life-years lost to stroke. Its surgical and medical treatment represents a multidisciplinary effort. Due to the complexity of the disease, the management remains difficult to standardise and quality of care is accordingly difficult to assess. OBJECTIVE: To create a registry to assess management parameters of patients treated for aSAH in Switzerland. METHODS: A cohort study was initiated with the aim to record characteristics of patients admitted with aSAH, starting January 1st 2009. Ethical committee approval was obtained or is pending from the institutional review boards of all centres. In the study period, seven Swiss hospitals (five university [U], two non-university medical centres) harbouring a neurosurgery department, an intensive care unit and an interventional neuroradiology team so far agreed to participate in the registry (Aarau, Basel [U], Bern [U], Geneva [U], Lausanne [U], St. Gallen, Zürich [U]). Demographic and clinical parameters are entered into a common database. DISCUSSION: This database will soon provide (1) a nationwide assessment of the current standard of care and (2) the outcomes for patients suffering from aSAH in Switzerland. Based on data from this registry, we can conduct cohort comparisons or design diagnostic or therapeutic studies on a national level. Moreover, a standardised registration system will allow healthcare providers to assess the quality of care.

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Authors	Collaborators
Bawarjan Schatlo[1]	Stephan Jakob[2]
Christian Fung[2]	Michael Reinert[2]
Ali-Reza Fathi[3]	Jürgen Beck[2]
Martin Sailer[4]	Yvan Gasche[1]
Kerstin Winkler[5]	Asita Sarrafzadeh[1]
Roy Daniel[6]	Vitor Mendes-Pereira[1]
Philippe Bijlenga[1]	Marc Levivier[6]
Martin Seule[7]	Sofia Nistor[6]
Daniel Zumofen[4]	Peter Ahlborn[7]
Marc Levivier[6]	Christoph Woernle[5]
Gerhard Hildebrandt[7]	
Luigi Mariani[4]	
Javier Fandino[3]	
Andreas Raabe[2]	
Emanuela Keller[5]	
Karl Schaller[1]	

Institutions:

(1) Department of Neurosurgery, Geneva University Hospital, Switzerland

(2) Department of Neurosurgery, Inselspital, Bern, Switzerland

(3) Department of Neurosurgery, Kantonsspital Aarau, Switzerland

(4) Department of Neurosurgery, Basel University Hospital, Switzerland

(5) Department of Neurosurgery/Neurointensive Care Unit, University Hospital of Zürich, Switzerland

(6) Department of Neurosurgery, Lausanne University Hospital, Switzerland

(7) Department of Neurosurgery, Kantonsspital St. Gallen, Switzerland

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Correspondence and reprints:
Karl Schaller, MD
Department of Neurosurgery
Hôpitaux Universitaires de Genève
Faculty of Medicine, University of Geneva
Rue Micheli-du-Crest 24
1211 Geneva 14
Switzerland
Phone +41-22-3728201
Fax +49-22-3728225
Email karl.schaller@hcuge.ch

Abstract

Background

Aneurysmal subarachnoid hemorrhage (aSAH) is the most prevalent form of hemorrhagic stroke and accounts for a large proportion of productive life years lost to stroke. Its surgical and medical treatment represents a multidisciplinary effort. Due to the complexity of the disease, the management remains difficult to standardize and quality of care is accordingly difficult to assess.

Objective

To create a registry to assess management parameters of patients treated for aSAH in Switzerland.

Methods

A cohort study was initiated with the aim to record characteristics of patients admitted with aSAH between January 1st and December 31st 2009. Ethical committee approval was obtained or is pending from the institutional review boards of all centers. In the study period, seven Swiss hospitals (five university (U), two non-university medical centers) harboring a neurosurgery department, an intensive care unit and an interventional neuroradiology team so far agreed to participate in the registry (Aarau, Basel (U), Bern (U), Geneva (U), Lausanne (U), St. Gallen, Zürich(U)). Demographic and clinical parameters are entered into a common database.

Discussion

This database will soon provide (1) a nationwide assessment of the current standard of care and (2) outcome of patients suffering from aSAH in Switzerland. Based on data from this registry, we can conduct cohort comparisons or design diagnostic or therapeutic studies on a national level. Moreover, a standardized registration system will allow healthcare providers to assess the quality of care.

Key words: cerebral aneurysm, Switzerland, subarachnoid hemorrhage, clipping, coiling

Running title: Swiss subarachnoid hemorrhage study

Introduction

Overview and socioeconomic impact

SAH is type of hemorrhagic stroke which occurs due to rupture of an intracranial aneurysm in 85% of cases. The incidence of aSAH between regions of the world is highly variable (from 3 in parts of South America to over 20 per 100,000 person-years in Japan) (de Rooij, Linn et al. 2007). aSAH represents 5% of all cerebrovascular accidents. In contrast to the more prevalent ischemic stroke which affects an older age-group, half of the patients suffering from aSAH are younger than 55 years. aSAH thus accounts for a quarter of all productive life years lost to stroke (Johnston, Selvin et al. 1998). Patients admitted and diagnosed with aSAH have long hospital stays (average in patients over 65 years: 22 days (Taylor, Yuan et al. 1997)) and most are at least temporarily monitored in a neuro-intensive care unit. The cost of hospitalization of a "low severity" case of aSAH was estimated to be 35,000$ in the US (Maud, Lakshminarayan et al. 2009). The healthcare cost of aSAH amount to an estimated 437 million EUR per year for Germany alone (Dodel, Winter et al. 2010). In addition to the socioeconomic impact, the disease affects the quality of life of more than nine out of ten patients even one year after discharge (Meyer, Ringel et al. 2010).

Necessity of a nationwide registry

The management of aSAH in Switzerland has not been assessed on a national level to date. We united large neurovascular centers in Switzerland to create a registry for aSAH. This registry helps collect clinical and management data from different centers and pools it in one common database. It may provide referring caregivers and healthcare providers with a critical tool to assess the quality of care in a disease which has a high socio-economic burden. Moreover, it may serve as a tool to foster scientific collaboration and address a number of remaining questions about the management of aSAH in the future.

Dilemmas in the management of aSAH

aSAH has a poor prognosis, with a mortality of about 40% and morbidity including neurological deficits affecting about one third of patients . Prognosis is not only limited by the bleed itself with the associated early brain injury, but also by conditions such as hydrocephalus, delayed

ischemic neurological deficits and extracranial disease (Macdonald, Pluta et al. 2007). The following points briefly illustrate exemplary domains where further large-scale studies are necessary to answer imminent questions on the optimal management of aSAH. These and other points have been included in the current registry.

Aneurysm treatment

Rebleeding is the most dangerous complication of aSAH and occurs mostly within hours of days of the initial bleed. Therefore, it is mandatory to perform aneurysm treatment early to prevent re-rupture. The main options for aneurysm occlusion are surgical clipping, endovascular coiling or stenting. The treatment decision is commonly taken after interdisciplinary discussion based on aneurysm size, location and the patient's constitution. Surgical as well as interventional techniques have undergone significant development in recent years, prompting a continuous critical assessment of safety, efficacy and longterm outcome. Especially for stenting there is relatively little data to compare its risks and benefits to coiling or clipping.

Management of hydrocephalus

About 15% of patients develop acute hydrocephalus after aSAH (Graff-Radford, Torner et al. 1989). The standard treatment for acute hydrocephalus cerebrospinal fluid drainage by an external ventricular drain. However, recent studies have re-assessed the possibility of lumbar drainage. The optimal management of subacute or late hydrocephalus still remains a matter of debate. Uncertainty also remains about the best timing to perform surgery for a ventriculo-peritoneal shunt versus trying repeated lumbar punctures.

Detection of delayed ischemic deficits

Delayed ischemic deficits occur in a significant proportion of patients after aSAH and CT-proven infarcts occur in 40% (Rabinstein, Weigand et al. 2005). It is suspected that the number of patients suffering cerebral ischemia after aSAH has been underestimated. Both the prevention, detection and the treatment of delayed ischemia remain unsolved problems: A number of diagnostic tools to monitor cerebral blood flow on the bedside are available, but their respective limitations have hitherto prevented universal acceptance (Vajkoczy, Horn et al. 2003). The main drawback of most bedside methods is their inability to monitor cerebral blood flow in the whole

brain. Moreover, recent insights into alterations of cerebral blood flow due to waves of depolarization as precursors of ischemia may improve the early detection of delayed ischemic events. However, the development of practicable and widely available monitoring equipment is still in the experimental stages (Dreier 2011).

Prevention of delayed ischemic deficits

The fact that delayed ischemia after aSAH occurs several days after the bleed in patients who are already in the hospital makes this complication potentially preventable. Most of the early efforts in preventing these deficits were aimed at the treatment of angiographic cerebral vasospasm which occurs between days 4 and 14. Interestingly, the reduction of angiographic spasm has so far not translated to an improvement in patient outcome (Macdonald, Higashida et al. 2011). The calcium-channel blocker nimodipine has a modest impact on delayed cerebral ischemia and is the only pharmaceutical treatment approved for the treatment of delayed cerebral ischemia and vasospasm (Dorhout Mees, Rinkel et al. 2007). However, its side effects, particularly systemic hypotension, significantly limit its use in this patient population where therapeutic hypertension is mandatory. Local delivery of vasodilators such as nicardipine pellets was found to be of benefit in patients undergoing surgery for aSAHa (Barth, Capelle et al. 2007).

Outcome measures

aSAH for the larger part affects people in their working age. Therefore, even slight neurological disturbances can have a major impact on their ability to return to their previous occupation. Some authors argued that the presumed lack of efficacy for drugs reversing delayed cerebral vasospasm may be due to the absence of adequate outcome measures. Such outcome measures include a thorough neurological test battery as well as quality of life parameters. A registry on a national level could have a sufficient caseload to help develop and validate testing batteries including quality of life questionnaires such as the modified Rankin Scale or the Glasgow Outcome Scale Extended (Wilson, Pettigrew et al. 1998). Our hope is also that by standardizing outcome measures at a later point in this study, follow-up will ultimately improve.

Materials and Methods

Neurovascular teams at seven Swiss hospitals (five university (U), two non-university medical centers) which treat patients with aSAH held two initiation meetings in 2009 and 2010 (Aarau, Basel (U), Bern (U), Geneva (U), Lausanne (U), St. Gallen, Zürich(U)). Participating centers have a neurosurgery department, an intensive care unit and an endovascular team and are tertiary referral centers within Switzerland. The Swiss SOS registry is designed as a multicentre database with the same parameters (an overview is provided in table 1, for a complete reference see supplementary material 1) which each participating center manages independently. Anonymized demographic and clinical data are recorded in prospective manner, or where necessary, retrospectively for cases admitted since 01.01.2009. Ethical committee approval was obtained or is pending from the institutional review boards of all centers.

Patient recruitment

All patients admitted with a diagnosis of aSAH at one of the participating centers are entered into the local database. Patient data is pseudonymized. The local databases can be fused into a common centralized file.

Statistical analysis

Statistical analysis and data quality evaluation will be performed by a dedicated statistician.

Discussion

Our aim is to create an observational database on clinical management aspects of aSAH. The severity of the disease and its many complications make aSAH a challenging disease to treat from the first day to the day where the patient can leave the hospital, often weeks later. aSAH patients can be categorized by clinical status at admission (World Federation of Neurological Surgeons Scale (Rosen and Macdonald 2005)), severity of hemorrhage (Fisher scale (Fisher, Kistler et al. 1980)), aneurysm localization, presence of hydrocephalus or epilepsy or even extracranial disease (e.g. cardiac arrhythmia, pulmonary edema). While all participating Swiss centers have a “high volume” (Barker, Amin-Hanjani et al. 2003) with more than 20 patients per year, but each patient requires individualized decision-making based on a multitude of parameters. Moreover, the patient is treated by a team including among others neurosurgeons, neuro-interventionalists, neuro-intensivists and anesthesiologists. The evident lack of consensus on optimal management prompts a large-scale effort which cannot be mustered by one center

alone. For a population of about eight million, Switzerland has several neurovascular centers with a high standard, and a common Swiss registry can serve multiple purposes:

Assessment of the status quo

The management of patients with aSAH in Switzerland has not yet been explored on a national level. A common database will help provide such an assessment.

Simplicity and standardization

Our aim is to provide a database on aSAH which has a limited number of parameters and remains simple in its use. The parameters should be applicable in a similar manner by investigators from all centers and are therefore standardized.

Socioeconomic parameters and patient outcome

Age, duration of hospitalization (total duration and intensive care unit) and modified Rankin Scale at discharge as well as at follow-up are recorded in the database and give an estimate of the immediate socioeconomic burden of aSAH. Moreover, the database can be extended using quality of life measures.

Clinical status and management

Basic information on clinical status at admission, treatment modalities as well as delayed complications are recorded. The presence of multiple aneurysms and their impact on management can be derived from the datasets.

Quality of care

In response to increasing medical knowledge, medical disciplines are increasingly evolving towards areas of subspecialty. This tendency is also tangible in Switzerland where federal efforts are focused towards developing reference centers which are staffed and equipped appropriately and which will receive patients with a specific pathology from beyond their traditional recruitment area.

Healthcare providers are also asked to justify expenses by documenting the quality of care. The ability to provide outcomes in a standardized manner will enable clinicians to anticipate requests

of insurers and public institutions particularly. This is particularly important since the costs of neurointensive care management are high and medical evidence is often lacking to support our individually-based treatment decisions.

Critical mass for research and further studies

Swiss neurovascular centers traditionally have shown a strong interest in the improvement of patient care through scientific research. To unite several high-level neurovascular centers may improve the visibility of a geographically limited community with similar research interests. The coordination for larger-scale studies or translational research efforts could be facilitated.

Funding

Currently, the Swiss SOS is a loose framework of a "neurovascular interest group". At present, no funding was applied for. As the first results of the collaboration will surface, hypotheses for potential scientific applications will be discussed and funding will be applied for to answer specific questions or conduct a project of common interest.

Limitations

At the beginning, our database will be retrospective and observational. The assessed parameters (provided in table 1) are of relative simplicity in order to limit time and expenses for the investigators. In the first phase of the project, there will be no study nurse due to the lack of starting funds as described above.

Conclusion

The creation of a national network for aSAH is a logical step forward in documenting treatment and outcome for a complex disease. The first goal is the improvement of patient management by standardization and comparability. Furthermore, the registry may serve as an initiator for studies with scientific hypotheses regarding diagnosis and treatment of aSAH.

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Table 1: Simplified overview of basic parameters

Patient	Unique ID (algorithm exists) Age at ictus Sex Female Male
Date of...	Ictus Admission Discharge ICU days
Clinical status at admission	mRankin before ictus GCS New focal neurological deficit Yes No New cranial nerve deficit Yes No
Radiology	SAH – blood distribution (Fisher scale) Location of the aneurysm Side R L Largest diameter (mm)
	Other aneurysms:
Clinical status at discharge	mRankin GCS New focal neurological deficit Yes No New cranial nerve deficit Yes No
Treatment	Coil Clip Stent EVD Hemicraniectomy Other None
Hydrocephalus	...requiring VP shunt Yes No
Vasospasm	Underwent balloon dilation
	Permanent delayed neurological deficit
Long term outcome (at year 1)	mRankin GCS New focal neurological deficit Yes No New cranial nerve deficit Yes No
Long term outcome (at year 5)	mRankin GCS New focal neurological deficit Yes No New cranial nerve deficit Yes No